A WNT protein therapeutic improves the bone-forming capacity of autografts from aged animals.

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Public Summary:
Autografts tend to be unreliable in older patients. Some of these age-related skeletal changes appear to be attributable to a decline in endogenous WNT signaling. We used a functional in vivo transplantation assay to demonstrate that the bone-forming capacity of an autograft can be traced back to a Wnt-responsive cell population associated with the mineralized bone matrix fraction of a bone graft. Micro-CT imaging, flow cytometry and quantitative analyses demonstrate that this mineralized fraction declines with age, along with a waning in endogenous Wnt signaling; together these factors contribute to the age-related deterioration in autograft efficacy. Using a lipid formulation to stabilize the hydrophobic WNT3A protein, we demonstrate that osteogenic capacity can be restored by incubating the bone graft ex vivo with WNT3A. Compared to control bone grafts, WNT-treated bone grafts give rise to three times more bone. These preclinical results establish a pivotal role for WNT signaling in the age-related decline of autologous bone grafting efficacy, and demonstrate a means to restore that efficacy via local, transient amplification of endogenous Wnt signaling.

Scientific Abstract:
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